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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/661,428 | 09/11/2003 | Lars-Erik Peters | 1995/US/2 | 8089 |

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| EXAMINER | |
|---|---|
| TUNG, JOYCE | |
| **ART UNIT** | **PAPER NUMBER** |
| 1637 | |

DATE MAILED: 08/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/661,428 | PETERS, LARS-ERIK | |
| | Examiner | Art Unit | |
| | Joyce Tung | 1637 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *21 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-38* is/are pending in the application.

4a) Of the above claim(s) *1-14 and 36-38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/11/2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

The applicant's response filed 6/21/2006 to the Office action mailed 4/18/06 has been entered. Claims 1-38 are pending.

### *Election/Restrictions*

1. Applicant's election without traverse of Group II, claims 15-35 in the reply filed on 6/21/06 is acknowledged.

2. Claims 1-14 and 36-38 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 6/21/06.

### *Claim Rejections - 35 USC § 112*

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 20-21, 23-25, 27-29 and 32-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 27-29 are vague and indefinite because of the phrase "the anionic polysulfate". It is unclear what is the antecedent basis for the phrases.

b. Claims 20-21, and 23-25 are vague and indefinite because it is unclear what is the unit for the molecular weight.

c. Claims 28, 29, and 32-35 are vague and indefinite because of the phrase "consisting essentially of". The phrase "consisting essentially of" is improper Markush language. It is suggested to amend to "consisting of".

***Claim Rejections - 35 USC § 103***

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 15-16 and 19-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fischer et al. (Biochemistry, 1989, Vol. 28, 1989, pg. 5219-5226), in view of Gelfand et al. (5,693,517, issued December 2, 1997) and Stratagene Catalog, 1988.

Fisher et al. disclose a polyanion, which is an anionic polyester of L-malic acid, and inhibits the activity of the DNA polymerase α. Poly (L-malate) reversibly binds to DNA polymerase α. The major size corresponds to a molecular mass of 40-50 kDa. (See page. 5219). The teachings of the size of the polyanion are within the range of the molecular weight as recited in claims 20-21. Fisher et al. also disclose that poly(L-malate) forms complexes with DNA polymerase α of high affinity, the inhibition of the DNA synthesis is the competition with the

substrate of DNA at the presence of the Klenow fragment (of *E.coli* DNA polymerase I) (See pg. 5225, column 1, first paragraph).

Fisher et al. do not disclose the kit containing all elements used in the method.

Stratagene catalog discloses kit containing all the elements needed for performing a method.

Fisher et al. also do not disclose that the Klenow fragment (of E.coli DNA polymerase I) is thermostable polymerase.

Gelfand et al. disclose thermostable DNA polymerase used in high temperature cDNA synthesis (See column 3, lines 54-62). The thermostable DNA polymerase is from *Thermus thermophilus* (See column 15, lines 52-58, column 16, lines 60-67).

One of ordinary skill in the art would have been motivated to make the kit including the polyanion of Fisher et al. because the polyanion of Fisher et al. binds to a DNA polymerase reversibly in polynucleotide synthesis mixture, the Klenow fragment (of *E.coli* DNA polymerase I) and thermostable polymerase have the same function as taught by Gelfand et al. in that the thermostable DNA polymerase used in the method of Gelfand improves the method for a one enzyme, one tube, coupled reverse transcription/amplification assay in which the method offers enhanced sensitivity, simplicity and specificity over current method (See column 3, lines 54-62). Thus, one of ordinary skill in the art at the time of the instant invention would have been motivated to make the kit including the polyanion which could be used in reversibly binding to the thermostable polymerase and an appropriate polymerase reaction buffer because it was routine practice to make a kit including all elements needed for performing a method as taught by Stratagene catalog. It would have been prima facie obvious to make the kit as claimed.

7. Claims 22-25 and 32-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fischer et al. (Biochemistry, 1989, Vol. 28, 1989, pg. 5219-5226) in view of Gelfand et al. (5,693,517, issued December 2, 1997), Stratagene Catalog, 1988 and Mullis et al. (4,965,188, issued Oct. 23, 1990).

The teachings of Fisher et al., Gelfand et al. and Stratagene Catalog are set forth in section 6 above.

None of references cited above disclose a polymerase reaction buffer having monovalent cations between 35-60 mM, at least one dNTP, a template nucleic acid molecule and primers.

Mullis et al. disclose a polymerase chain reaction buffer containing monovalent cations, 50mM KCl, at least one dNTP, template and primers (See column 29, lines 10-32). The DNA polymerase is from *Thermus aquaticus* (See column 29, lines 19).

None of the references above disclose a composition including all elements as needed for performing the method.

However, Stratagene catalog discloses a kit containing all elements as needed for conveniently performing a method. The kit has the same function as the composition, which also is used for conveniently performing a method.

One of ordinary skill in the art would have been motivated to make the composition including the polymerase chain reaction buffer of Mullis et al. because the buffer of Mullis et al. is used in a polymerase chain reaction for the synthesis of the desired nucleic acid sequences (See the abstract) and Stratagene catalog discloses a kit which has all elements needed for conveniently performing a method. It would have been prima facie obvious to make the

composition including the polymerase chain reaction buffer and other elements needed for conveniently performing the polynucleotide synthesis.

8. Claims 17, 26, and 29-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fischer et al. (Biochemistry, 1989, Vol. 28, pg. 5219-5226), Gelfand et al. (5,693,517, issued December 2, 1997) in view of Stratagene Catalog, 1988 as applied to claims 15-16, 19-21, 22-25 and 32-35 above, and further in view of Shimada et al. (Nucleic acids research, 1978, Vol. 5(9), pg. 3427).

The teachings of Fisher et al. and Stratagene Catalog are set forth in section 6 above.

Fischer et al. do not disclose polyvinyl sulfate, dextran sulfate and heparin.

Shimada et al. disclose that polyvinyl sulfate, dextran sulfate and heparin inhibit the activity of DNA polymerase $\alpha$ (See pg. 3427, the Abstract).

Shimada et al. do not disclose the concentration of polyvinyl sulfate, dextran sulfate and heparin used for the inhibition of DNA polymerase $\alpha$.

One of ordinary skill in the art at the time of the instant invention would have been motivated to include polyvinyl sulfate, dextran sulfate and heparin in a kit or a composition for polynucleotide synthesis because polyvinyl sulfate, dextran sulfate and heparin inhibit the activity of the DNA polymerase $\alpha$ with a certain amount of the concentration as taught by Shimada et al. (See pg. 3432). In addition, one of ordinary skill would have also been motivated to optimize the concentration of polyvinyl sulfate, dextran sulfate and heparin because this was routine practice in the art at the time of the invention. It would have been prima facie obvious to include these polyanions recited in claims 17, 26 and 28 with the concentration recited in claims 30-31 in the kit or the composition for polynucleotide synthesis.

9. Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Fischer et al. (Biochemistry, 1989, Vol. 28, 1989, pg. 5219-5226), Gelfand et al. (5,693,517, issued December 2, 1997) in view of Stratagene Catalog, 1988 and Yang (6,274,353, issued August 14, 2001).

The teachings of Fisher et al. and Stratagene Catalog are set forth in section 6 above. None of the references discloses the kit for polynucleotide synthesis comprising at least one nucleotide 5'-triphosphate.

Yang discloses a method of polynucleotide synthesis (See the Abstract) and a kit comprising nucleotide 5'-triphospahte (See column 30, claim 10).

One of ordinary skill in the art at the time of the invention would have been motivated to include nucleotide 5'-triphosphate in the kit for polynucleotide synthesis because by using nucleotide 5'-triphospahte in polynucleotide synthesis method of Yang, the method of Yang improves the specificity and sensitivity of the method (See column 4, lines 17-18). It would have been prima facie obvious to have nucleotide 5'-triphosphate in the kit.

10. Claims 27-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fischer et al. (Biochemistry, 1989, Vol. 28, 1989, pg. 5219-5226), Gelfand et al. (5,693,517, issued December 2, 1997) in view of Stratagene Catalog, (1988) and Yoshitaka Aoi et al. (Journal of Medicine, Vol. 12 (2&3), 1981. pg. 127-145).

The teachings of Fisher et al. and Stratagene Catalog are set forth in section 6 above. None of the references discloses sulfated oligo or polysaccharide, which is selected from the group recited in claim 28.

Yoshitaka Aoi et al. disclose glycosaminoglycans, which inhibit DNA synthesis of virus transformed cells (See pg. 127, the Abstract).

One of ordinary skill in the art at the time of the invention would have been motivated to include glycosaminoglycans in a composition for polynucleotide synthesis because as indicated by Yoshitaka Aoi et al. glycosaminoglycans inhibit more efficiently DNA synthesis of virus transformed cells (See pg. 127, the Abstract). It would have been prima facie obvious to include glycosaminoglycans in the composition for polynucleotide synthesis.

**Summary**

11. No claims are allowable.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joyce Tung whose telephone number is (571) 272-0790. The examiner can normally be reached on Monday - Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Joyce Tung
August 18, 2006

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER

8/24/06